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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/894,208      | 06/28/2001  | James G. Nadeau      | P-4756D2            | 3585             |

7590 07/12/2002  
Becton, Dickinson and Company  
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EXAMINER

GUNTER, DAVID R

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1634

DATE MAILED: 07/12/2002

4

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/894,208

Applicant(s)

NADEAU ET AL.

Examiner

David Gunter

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 28 June 2001.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 36-47 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 36-47 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

Art Unit: 1634

### DETAILED ACTION

1. The examiner acknowledges the applicant's claim to priority for the instant application as a division of U.S. Patent Application 09/550,061, filed June 8, 2000.

#### *Claim Objections*

2. Claims 37 and 39 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claims, or amend the claims to place the claims in proper dependent form, or rewrite the claims in independent form.
  - a. Regarding Claim 37, wherein the double-stranded reporter moiety is produced upon hybridization of the report moiety to the complement of the adapter sequence, the claim is redundant. This limitation has already been recited in Claim 36 (c), and Claim 37 does not recite any further limitation beyond that found in 36 (c).
  - b. Regarding Claim 39, wherein the double-stranded reporter moiety is produced upon synthesis of a complement of the reporter moiety, the claim is redundant. Claim 36 (b) recites synthesis of a complement to the adapter sequence, which is hybridized to the reporter to form a double-stranded reporter moiety in Claim 36 (c). Claim 39 as written does not recite any further limitations beyond those found in Claims 36 (b) and (c). If the claim is meant to recite that the complement to the single-stranded reporter moiety is synthesized *in situ* rather than synthesized as a complement to another strand and

Art Unit: 1634

subsequently hybridized to the reporter, the claim should be amended to make this fact clear.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 36-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Regarding Claim 36, the claim recites a series of steps in which primers are hybridized to target nucleotide sequences and extended. For the purposes of examination, it is assumed that the newly synthesized nucleic acid is dissociated from its template through the use of heat or other means prior to the hybridization of the subsequent primer. However, these denaturation and re-annealing steps are not clearly recited in the claim, and so the nature of the association among the primers, templates, and newly synthesized nucleic acid molecules is not clear.

b. Regarding Claim 36 (a), the phrase “the adapter sequence produces a 5’ overhang” is confusing. The word “produces” implies synthesis of an overhanging nucleotide, whereas figure 1A indicates that the 5’ overhang is comprised of the 5’ region of the signal primer. This 5’ region is not complementary to the target nucleic acid and therefore does not hybridize to the target and results in the formation of an overhang. The word “produces” should be replaced with “comprises.”

Art Unit: 1634

- c. Regarding Claim 38, the meaning of the term “molecular beacon” is not clear because it is not defined in the claims or specification.
- d. Regarding Claim 40, the phrase “specialized sequence” is confusing because it is not clearly defined in the claim. Furthermore, neither “specialized sequence” nor “secondary structure” have antecedent basis in Claim 36.
- e. Regarding Claim 46, it is unclear whether the “multiple signal primers” anneal to a single target sequence or to each of multiple target sequences. The claim should be amended to indicate the nature of the association between the primers and their target or targets.

The following is a statement of reasons for the indication of allowable subject matter:

The claims of the instant application recite a method for detecting a nucleic acid target sequence comprising (a) hybridizing a signal primer comprising an adapter sequence to the target sequence such that the adapter sequence produces a 5' overhang; (b) synthesizing a complement of the adapter sequence by extension of the hybridized target sequence; (c) hybridizing a reporter probe comprising a reporter moiety to the complement of the adapter sequence, whereby a double-stranded reported moiety is produced, and; (d) detecting the double-stranded reporter moiety as an indication of the presence of the target sequence .

The art most similar to the instant application is USPN 5,525,494, issued June 11, 1996 (hereinafter referred to as USPN '494). USPN '494 discloses a method for detecting a nucleic acid sequence comprising a “first primer” (analogous to the signal primer of the instant

Art Unit: 1634

application) comprising a target nucleotide binding moiety and a polynucleotide tail (analogous to the adapter sequence of the instant application). The first primer is hybridized to the target nucleotide sequence and extended to produce a “first primer extension product.” The first primer extension product is dissociated from the target nucleic acid and then hybridized to an amplification primer that is then extended to form an “amplification primer extension product.” The amplification primer extension product is then dissociated from the first primer extension product and hybridized to “a detection primer conjugated to, for example, a fluorophore” (analogous to the reporter probe of the instant application). (Column 2, lines 12-48; Column 4, lines 6-10).

USPN ‘494 discloses many embodiments similar to those of the instant application, including:

- a. the embodiment in which the double-stranded reporter moiety is produced (Claim 37 of the instant application; USPN ‘494 Column 2, lines 12-48 and Column 4, lines 6-10).
- b. the embodiment in which the double-stranded reporter moiety is produced upon synthesis of a complement to the reporter moiety (Claim 39 of the instant application; USPN ‘494 Column 2, lines 12-48 and Column 4, lines 6-10).
- c. the embodiment in which a change in fluorescence is detected (Claim 43 of the instant application; USPN ‘494 Column 4, lines 6-21).
- d. the embodiment in which the method comprises multiple signal primers, each signal primer having a separately detectable adapter sequence (Claim 46 of the instant application; USPN ‘494 Column 3, lines 42-60 and Column 4, lines 54-64).

Art Unit: 1634

- e. the embodiment in which each signal primer hybridizes to a different sequence variant of the target sequence (Claim 47 of the instant application; USPN '494 Column 3, lines 42-60 and Column 4, lines 54-64).

USPN '494 discloses the embodiment in which the first primer (signal primer) is modified at the 5' terminus so that the polynucleotide tail (adapter sequence) cannot serve as a template for a DNA polymerase. This modification is disclosed as critical to the method because in the absence of such a modification the DNA polymerase would "cause amplification of the polynucleotide tail as well as the extended target binding portion of the primer. In such a case ... competition for attachment to the further species (for example to a solid phase or signaling moiety) arises which thereby inhibits binding" (Column 2, lines 7-14).

This modification of the first primer (signal primer) to prevent its amplification is a central aspect of USPN '494 and is a significant departure from the method of the instant application. The instant application relies on DNA polymerase to synthesize complements to the adapter sequence in order to allow detection of the target nucleic acid sequence. For this reason, USPN '494 "teaches away" from the instant application.

4. **No claims are allowed.** However, claims are free of the prior art and can be placed in condition for allowance by addressing the 35 U.S.C. 112 issues.

Art Unit: 1634

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David R. Gunter whose telephone number is (703) 308-1701.

The examiner can normally be reached on 9:00 - 5:00 M - F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 746-9212 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0198.



David R. Gunter, DVM, PhD  
July 10, 2002

